Best Poster Award – Second Prize

Bile Acids as Novel Vascular Signalling Molecules and Therapeutic Target

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Background: Bariatric surgery (Roux-en-Y gastric bypass, RYGB) reduces cardiovascular mortality and improves HDL-mediated vasoprotection. Bile acids (BA) are emerging as signalling molecules controlling cardiometabolic health. Plasmatic BA circulate partly bound to HDL.

Purpose: We tested whether and how changes in composition of BA bound to HDL (HDL-BA) after RYGB contribute to HDL-mediated endothelial protection.

Methods: HDL isolated from 47 obese patients before and 1 year after RYGB were tested for their protective properties using human endothelial cells *in vitro*. HDL BA and lipid composition was quantified by liquid chromatography-mass spectrometry.

Results: At 1 year after RYGB, higher concentrations (up to 25%) of BA were bound to HDL with an increase on HDL of BA agonists either for nuclear farnesoid X receptor (FXR), e.g. cholic acid (CA) and chenodeoxy-CA (CDCA), or for membrane receptor TGR5, e.g. taurolitho-CA (TLCA). After RYGB, HDL levels were increased and HDL-mediated endothelial NO production, anti-apoptotic and cholesterol efflux capacity were restored. The composition-function analysis showed that higher HDL-CA correlated with improved anti-apoptotic capacity. Further, RYGB improves the lipidomic profile of HDL with reduced cholesteryl esters and toxic ceramides, and increased anti-oxidant plasmalogens.

Conclusion: RYGB increases the concentration and improves the function and the molecular lipid composition of HDL. Interestingly, higher concentrations of BA bound to HDL after RYGB may mediate HDL's improved endothelial-protective effects via enhanced endothelial activation of FXR and TGR5. ■